Remarks

The rejection of claims 76-79, 81-86, 88-96 under Section 112, para. 1 has been overcome by amendment wherein the term "loosely packed, ordered array" has been deleted, as has the term "same distance from one another."

The provisional rejection on the grounds of nonstatutory obviousness-type double patenting of claims 76, 77, 79, 83, 86, 93, 95, 97, 99, 100, 102, 104, 107, 109, 114 over application Serial No. 11/436,718, of claims 76, 77, 79, 83-86, 88, 91-97, 9, 100, 102-104, 106-115 over application Serial No. 11/436009, of claims 76-79, 81-86, 88-115 over application Serial No. 10/310,173, of claims 76-79, 81-86, 88-115 over application Serial No. 11/436,717, and of claims 76-79, 81-86, 88-115 over application Serial No. 10/424,662 is overcome by the terminal disclaimers filed previously.

The Examiner has rejected claims 76, 77, 79, 83, 86, 89-93, 96, 97, 99-104, and110-115 under 35 U.S.C. 103(a) over Drmanac (EP 0392546A2) in view of Dower. Claim 79 now recites: "said particles form several planar hexagonal crystalline configurations." The formation of hexagonal crystalline configurations is in the application specification and is not disclosed or suggested in Drmanac, where the particles are "mixed and spread in a random monolayer" (Office Action page 11) on a filter, and that HA's with the particles can be subdivided. This means the particles in Dower are not in any type of order.

The Examiner rejected claims 76-79, 81-84, 86, 88-106, and 108-115 under 35 USC Section 103(a) over Margel in view of Singer et al. and further in view of Dower. Margel is directed to a method of attaching microspheres to a substrate, as set forth in the title, for the purpose of chemically modifying a substrate surface. Example 31 contains the only mention in Margel's disclosure that the immobilized microparticles can be used in an assay (and is the only part which can logically be used in the obviousness rejection in combination with other references). Example 31 describes the "wells of Eliza (sic) titer plates coated with polyacrolein microspheres of 800 Angstrom units average diameter" being incubated with sheep immunoglobulins. Margel et al. does not disclose any order in the attachment, including a hexagonal crystalline configuration, or "distinguishing different particles from each other" (claim 76). Example 31, in fact

teaches away from optical detection of assay signals of individual microparticles immobilized on the substrate surface. Specifically, Example 31 describes the determination of the reactivity of the sheep immunoglobulins with biotinylated antibodies directed against these immunoglobulins by way of reacting the antibodies with Extravidin peroxidase, which produces a detectable chromogenic substance, in accordance with standard ELISA protocols. However, this chromogenic stain diffuses into solution, and cannot be associated with individual microparticles – rather, an assay signal is recorded from the entire well, not from individual microparticles, for example, by determining optical absorbance, in accordance with standard methods of the art. The use of labeled microparticles (labeled with dyes as in Singer et al.) for the modification of the ELISA plate surface as in Example 31 of Margel would be of no benefit. In fact, it conceivably would interfere with the detection of the chromogenic substrate by introducing additional spectral signatures into the assay.

Further, to ensure at least a reasonable performance of the modified substrate surfaces in the applications considered by Margel, microparticles selected for coating of the substrate must be small. In fact, as described in Margel, Example 31, even the use of microparticles of only 800 A in diameter for the intended purpose of modifying the walls of an ELISA plate, significantly ***diminishes*** assay sensitivity (by ***increasing*** the detection limit) when compared to plates modified by coating with a solution that does not contain microparticles. Yet, even the microparticles of Example 31 are significantly smaller than the minimal size required to render them distinguishable, as required in the claims.

Contrary to the Examiner's assertion that "it would have been obvious ... to modify the method of Margel with microparticles having detectably distinct spectral characteristics of a plurality of dyes incorporated into the microparticles and each microparticle is labeled with a different target complement for detecting different target materials in a sample as taught by Singer ..." this modification would have been of no benefit and, even if made, would not yield the invention. In Margel the particles in Example 31 are coated on the surface of a well and thus are not in "planar array." And the particles in Margel, combined with Singer et al., would not be identifiable and distinguishable. Singer et al. relates to "methods for labeling or detecting one or more target materials using surface coated fluorescent microparticles with unique characteristics." *See* Singer et al. Abstract. Singer et al. discuss microparticle-labeled probes, but the microparticle-labeled probes are not in a "planar array," but rather the targets are

immobilized, and the microparticles serve only to permit the determination of the presence or absence of immobilized targets. There is no suggestion of optically detecting assay signals from microparticles in a planar array.

However, as with Margel, Singer et al. does not disclose the detection of assay signals and decoding signatures from such microparticles, but only a method of "labeling or detecting one or more target materials" in a format wherein targets of interest are immobilized , and are then contacted with probes attached to fluorescently labeled microparticles and then "unbound probes are optionally removed from the sample by conventional methods such as washing. For detection of the target materials, the ***sample is illuminated with means for exciting fluorescence in the microparticle-labeled probes***.... [see col. 20, line 33, to col. 21, line 36]." Thus, in this part of Singer et al., neither the targets nor the probes are individually encoded, but rather, the presence or absence of fluorescence signal emitted as a "smear" in a well, by the microparticle-labeled probes is detected, to indicate the presence or absence of a target decorated with a probe. Distinguishing individual microparticles is not suggested or disclosed, in fact, the combination of Margel and Singer et al. is taught against, as described above.

Claim 79 now recites: "said particles form several planar hexagonal crystalline configurations." The formation of hexagonal crystalline configurations is in the application specification and is not disclosed or suggested in Drmanac, where the particles are "mixed and spread in a random monolayer" (Office Action page 11) on a filter, and that HA's with the particles can be subdivided. This prevents the particles from being in pre-designated positions.

This claim element is also not disclosed or suggested in Margel. As noted above, Ex. 31 is the only relevant example in Margel, and it merely states: "The wells of Eliza titer plates coated with polyacrolein microspheres of 800 Angstrom units average diameter were incubated at room temperature for approximately 15 minutes ...." No coating method, and certainly not ordered coating is described, thus the coating would be random and non-ordered. Example 1 also describes making a coating of glass discs with microshperes, but it is also clear here that the coating is random and the attachment of the microspheres is random.

The Examiner also rejected claim 85 over over Margel in view of Singer et al. and further in view of Dower and further in view of Nacamulli. This is a dependent claim

and is allowable for the reasons the independent claim it depends from is allowable.

In conclusion, all claims are allowable.